of the body away from ready access to antibodies. Immunological defenses are much less effective in large tumors, as antibodies cannot reach the inner malignant cells. Therefore, immunological defense in cancer (immunosurveillance) is much more effective in the beginning stages of cancer or after most of the tumor mass has been removed by surgery, radiation or chemotherapy. Unfortunately, the latter two modes of therapy may cause a pronounced reduction in the patient's immune capacity.

The human body is probably faced with numerous neoplastic mutations, but rarely develops clinical cancer. The successful operation of the nonspecific and specific immune system is probably largely responsible for this level of protection.

Research in this area has produced a number of recent advances in our understanding of cancer immunology. It is anticipated that this new knowledge will add to and modify the information in this epitome.

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Indoor Air Pollution: Effects on the Non-Smoker of Tobacco Smoke Indoors

Smoke from an idling cigarette, "sidestream smoke," contains almost twice the tar and nicotine as does smoke inhaled while puffing on a cigarette, "mainstream smoke."

Furthermore, the carbon monoxide in the air near a smoker can be increased from an atmosphere value of perhaps one to three parts per million (ppm) to transient peaks exceeding 90 ppm. Two other components of any tobacco smoke are hydrogen cyanide and nitrogen dioxide. The latter, an acutely irritating gas, exists in cigarette smoke in amounts 160 times greater than levels considered safe for extended exposure.

Thus, the tobacco smoking minority of our population is the source of a unique and hazardous form of indoor air pollution which can best be discussed by using such special terms as *sidestream, mainstream* and *passive* smoking. Tobacco smokers who smoke indoors clearly put upon their more numerous non-smoking colleagues by worsening allergic rhinitis, bronchitis, asthma and other respiratory diseases.

Passive smoking by the non-smoker in a poorly ventilated room or car has been shown to result in carboxyhemoglobin levels well within the range known to cause impairment of visual acuity and faulty time interval discrimination. It is possible that such levels could be lethal for the bystander who suffers from arteriosclerotic heart disease. It is no cause for wonder, then, that the Surgeon General of the United States has declared a Bill of Rights for the non-smoker.

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Coexistence of Asthma in Children with Cystic Fibrosis

A CHILD with such recurrent, chronic symptoms as cough at rest or exertion, wheezing, fever, dyspnea or nasal obstruction may well have asthma, cystic fibrosis or both. This similarity of symptoms is a reflection of similar responses to the pathophysiology involved in both diseases.

It is well known that bronchial obstruction in patients with asthma is due to bronchoconstriction, submucosal edema, and increased bronchial secretions, and that patients with cystic fibrosis have highly viscid secretions. What is usually not appreciated is that nearly 50 percent of children with cystic fibrosis have exercise-induced bronchoconstriction and that a significant number have improved pulmonary function after inhalation of the bronchodilators epinephrine and isoproterenol. Therefore, bronchoconstriction as well as abnormal bronchial secretions, play a role in the clinical symptoms of both asthma and cystic fibrosis.

Asthma has been reported to occur in 7 to 10 percent of children with cystic fibrosis. This is similar to the incidence of asthma in the pediatric population in the United States. Therefore, it is important to realize that in some patients, both cystic fibrosis and allergy may be causing the symptoms and that treatment for both is necessary.

Recently, Caplin et al found interesting similarities between aspirin-induced asthma and cystic

fibrosis. These include high incidence of nasal polyps, severe intractable pulmonary disease with wheezing, and serum and sputum factors which inhibit ciliary action. Further identification of this inhibitor may shed light on the pathogenesis of both diseases.

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Genetics in Atopy

THE HEREDITARY NATURE of atopic allergic states, such as hayfever, asthma and eczema, has been known for half a century. Vaz and Levine discovered that gamma E immunoglobulin (IgE) antibody production in inbred strains of mice was under two sets of genetic controls. One causes elevated serum IgE antibodies to many antigens and the second controls reagin-production response to only certain antigens. The latter, termed an Ir (immune response) gene was linked closely to the H-2 major histocompatibility locus in mice. Such Ir genes described earlier by McDevitt and Benacerraf responded to synthetic polypeptides or minute doses of protein antigens.

Levine et al noted that the protein antigen dosage of pollens that one person inhales during a whole pollen season is extremely small, for example, 1 μg of ragweed antigen E (AgE) during a three-month ragweed season in New York. They wondered if there was an immune response gene in certain persons which could respond with IgE production to ragweed AgE. In seven families with a propositus and several other members with ragweed hayfever, they found that persons with clinical hayfever and intense wheal and flare skin tests to ragweed AgE all had the same HL-A histocompatibility haplotype which they called the "hayfever haplotype." There was, however, no single common "hayfever haplotype" in the seven families. Of 26 members of the seven families with the "hayfever haplotype," 20 had clinical hayfever and positive ragweed AgE skin tests. None of 11 family members who had the other haplotype of the propositus (and lacked the "hayfever haplotype") had clinical hayfever. These results were highly significant statistically ($p<.01$). Furthermore, none of 20 family members with neither haplotype of the propositus had hayfever. The close association between HL-A haplotype, clinical hayfever, and IgE antibody production in successive generations in man resembled the immune response gene associated with H-2 histocompatibility loci in mice. These findings suggest that tissue typing of infants born into allergic families might identify those at risk from allergic disease.

Marsh et al surveyed a population of 105 unrelated ragweed sensitive patients with positive findings for ragweed AgE from skin and leukocyte histamine release tests. Seventeen of these patients were highly sensitive to a minor antigenic determinant of ragweed called Ra5 (molecular weight 4,700), 77 percent were Ra5-insensitive and ten had intermediate sensitivity. HL-A typing of this population showed a highly significant correlation between HL-A7 and closely related group tissue types and high sensitivity to Ra5 ($p<0.003$) relative to frequency of those tissue types in the Ra5-insensitive group. This suggested to them that a certain immune response gene located at or near an HL-A locus controlled the immune responsiveness of a person to ragweed Ra5.

Hamburger and Bazaral at the University of California, San Diego, reported that total serum IgE levels in 26 pairs of monozygotic twins were very close, while IgE levels in dizygotic twins varied as greatly as in the general population. They suggested that serum IgE level is controlled genetically, as in Levine and Vaz's first group of mice.

Intensive efforts are underway in many laboratories for a better understanding of the familial occurrence of allergy on the basis of immune response genes.

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